IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Ulf SCHRODER	Confirmation No: 6616
Appl. No.	: 09/926,001	
Filed	: September 17, 2001	
Title	: VACCINE COMPOSITION	
TC/A.U.	: 1645	
Examiner	: V.L. Ford	
Docket No.:	: SCHR3003/REF	
Customer No:	: 23364	

APPEAL BRIEF 37 CFR §41.37

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This brief on appeal is submitted along with the required fee. A petition for a two month extension of time and the appropriate fee is submitted herewith extending the period for filing the brief to October 28, 2004. The brief is timely filed.

Any addition fees necessary for this appeal may be charged against the undersigned's Deposit Account No. 02-0200.

(c)(1)(i). REAL PARTY IN INTEREST

The real party in interest is the Assignee of record, EUROCINE AB.

(c)(1)(ii). RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences with respect to the claimed invention which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal known to appellant, appellant's legal representative or assignee.

(c)(1)(iii). STATUS OF CLAIMS

This application contains 46 claims. Claims 1-10 have been canceled from the application. Claims 11-46 are pending, are finally rejected and are the claims on appeal.

(c)(1)(iv). STATUS OF AMENDMENTS

The amendment after Final Rejection filed on May 12, 2004, has been enter for the purpose of this appeal as indicated in the Advisory Action of August 18, 2004.

(c)(1)(v). SUMMARY OF CLAIMED SUBJECT MATTER

The claims on appeal relate to novel tuberculosis vaccine compositions comprising as adjuvant one or more substances selected from monoglyceride preparations having at least 80% monogylceride content and also containing fatty acids with an acyl chain containing one or more unsaturated bonds and as immunizing component, inactivated *Mycobacterium tuberculosis* bacteria. (Page 5, lines 7-23.)

In a preferred embodiment the *M. Tuberculosis* bacteria are heat killed or formalin killed. (Page 5, line 24.)

The adjuvant of the vaccine composition of the invention preferably has a monoglyceride preparation content of at least 90%, preferably at least 95%, and the

acyl chains of the monoglyceride preparation contains 8 to 20 carbon atoms, preferably 14 to 20 carbon atoms and the acyl chains optionally contain one or more unsaturated bonds. (Page 5, lines 25-29.)

The vaccine compositions may additionally contain pharmaceutical excipients including biocompatible oils. (Page 5, line 31.)

In a most preferred embodiment of the invention the TB vaccine composition comprises, as adjuvant, a mixture of mono-olein and oleic acid, and possibly soybean oil, and as immunizing component heat-killed *M. tuberculosis bacteria*. (Page 6, lines 4-6.)

The composition may be formulated into an aerosol spray or a nose-drop package. (Page 6, lines 10-14.)

The claims on appeal also are directed to a method of vaccinating a mammal against tuberculosis which comprises mucosal administration to the mammal of a protection-inducing amount of a TB vaccine composition according to the invention. (Page 6, lines 14-17.)

The effectiveness of the protection of the composition of the present invention is clearly shown in Figure 2 which shows that approximately 70% of the mice receiving heat-killed vaccine formulation according to the present invention were still alive when the experiment was terminated. In contrast, the groups receiving classical live BCG only approximately 10 of the mice were still alive when the experiment was terminated. (Page 7, lines 32-36.)

(c)(1)(vi). GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103 as unpatentable over Youmans et al. in view of Schroder is to be reviewed on this appeal.

The rejection of newly submitted claims 38-45 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder is also to be reviewed on this appeal.

The rejection of claims 11-37 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder and further in view of Van Nest et al is another rejection to be reviewed on this appeal.

The rejection of claims 38-46 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder and further in view of Van Nest et al is the last rejection to be reviewed on this appeal.

(c)(1)(Vii). ARGUMENT

The issue involved in all of the rejections on appeal is whether or not the claimed subject matter is prima facie obvious to one of ordinary skill in the art to which the invention pertains, at the time of the invention. This requires an interpretation of the prior art as a whole at the time of the invention. Basically, it is Applicants' position that the prior art has been improperly interpreted relying on Applicants' specification. That is, the rejections are based on improper hindsight.

In this regard, Applicants wish to direct the Board's attention to the decision of the CAFC In re Demibiczak, 50 USPQ2d 1614. Applicants believe that the present rejections do not establish that the claimed invention is prima facie obvious. The following is from the decision, pages 1616 -1618.

> Our analysis begins in the text of section 103 quoted above, with the phrase "at the time the invention was made." For it is this phrase that guards against entry into the "tempting but forbidden zone of hindsight," see Loctite Corp. v. Ultraseal Ltd.,781 F.2d861, 873, 228 USPQ 90, 98 (Fed. Cir. 1985), overruled on other grounds by Nobelpharma AB v. Implant Innovations, Inc., 141F.3d 1059, 46 USPQ2d 1097 (Fed. Cir. 1998), when analyzing the patentability of claims pursuant to that

> section. Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. See ,e.g., W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d1540, 1553, 220 USPQ 303, 313 (Fed. Cir. 1983).
>
> See also MPEP §2141.02 Differences Between Prior Art and Claimed Invention -
>
> A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) (Claims were directed to a process of producing a porous article by expanding shaped, unsintered, highly crystalline poly(tetrafluoroethylene) (PTFE) by stretching said PTFE at a 10% per second rate to more than five times the original length. The prior art teachings with regard to unsintered PTFE indicated the material does not respond to conventional plastics processing, and the material should be stretched slowly. A reference teaching rapid stretching of conventional plastic polypropylene with reduced crystallinity combined with a reference teaching stretching unsintered PTFE would not suggest rapid stretching of highly crystalline PTFE, in light of the disclosures in the art that teach away from the invention, i.e., that the conventional polypropylene should have reduced crystallinity before stretching, and that PTFE should be stretched slowly.).

Applying the above judicial standards to the outstanding rejections, Applicants most respectfully submit that the rejections do not establish a prima facie case of obviousness of the claimed subject matter and should be reversed.

The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103 as unpatentable over Youmans et al. in view of Schroder is not tenable because a prima facie case of obviousness for the claimed subject matter has not been established.

These claims have been rejected on the basis that the Examiner finds that it would have been prima facie obvious to add the monoglyceride preparation as taught by Schroder to the *Mycobacterium tuberculosis* vaccine of Youmans et al.

In this regard, the Board's attention is direct to the limitation in all the claims that the immunizing component is **inactivated *Mycobacterium tuberculosis***

bacteria. This is a claim limitation which cannot be ignored nor can the fact that Youmans et al clearly teach, see the abstract, that the dose response curves show dramatically that viable cells, which do not multiply in vivo, are several hundred times more effective immunizing agents against tuberculous infection than are autoclaved cells. Autoclaved cells are inactive cells. Thus, the clear teaching of Youmans to one of ordinary skill in the art is away from, that is, not to use inactivated bacteria in a vaccine as used in the present invention. This is supported by the vaccine in use, at the time of the invention, which one of ordinary skill in the art knows contains a viable strain.

As stated on page 2 of Applicants' specification, The BCG vaccine consists of a weakened strain of tuberculosis bacteria taken from a cow in 1908. The original bacteria used today were cultured for 13 years for the purpose of weakening their pathogenic characteristics in order to be used as live bacteria for parenteral vaccination of humans. Basically the same strain is used today as the only vaccine available against TB. Several pharmaceutical companies around the world produce the BCG vaccine. The BCG formulation used today consists of freeze-dried attenuated viable BCG vaccine in one container and another container with physiologically acceptable suspension media. Thus, at the time of the present invention one of ordinary skill would understand that viable and not an inactive strain would be used in the vaccine. There would be no motivation to use **inactivated *Mycobacterium tuberculosis* bacteria** in accordance with the presently claimed invention.

According to the Examiner, Youmans et al. teaches a tuberculosis vaccine comprising heat or chemically killed *Mycobacterium tuberculosis*. But in what context?

As would be appreciated by one of ordinary skill in the art to which the invention pertains, the paper by Youmans et al. contains a comparison between tuberculosis vaccine comprising either viable attenuated cells or heat or chemically killed cells. The results shown clearly demonstrate that living cells prove to be several hundred times more effective as immunizing agents against tuberculous infection than autoclaved cells or cells inactivate by chemical agents. This is a clear teaching that viable cells should be used to formulate a vaccine.

Actually, in the conclusion (p. 112, column 2, last sentence) it is stated that living and killed mycobacterial cells differ not only quantitatively in their capacity to immunize against tuberculous infection, but qualitatively as well, the living cells being far more effective as immunizing agents.

From the results of the study performed by Youmans et al a person skilled in the art will recognize the importance of using living attenuated mycobacterial cells for immunizing against tuberculosis infection. Thus, Youmans et al describe that *"The data clearly show that the response to immunization with both living and heat-killed cells is dose-dependent and that living cells are several hundred times more effective than heat-killed cells"* (see page 109, first column, lines 1-5 from the bottom). This finding has been used in standard vaccination programs against Tuberculosis for many years and as seen from a transcript from FDA's homepage www.fda.gov, the TB vaccines on the US market contain live BCG. The same applies also in European countries such as, e.g. in Denmark, where a vaccine against TB (tuberculosis) (BCG Vaccine "SSI") presently on the market contains freeze-dried living attenuated bacteria from Calmette Guerin.

Based upon the above, one of ordinary skill in the art, at the time of the invention and considered the teachings of the prior art as a whole, would be lead to use living cells and not the inactivated cells used in the present invention. Thus, there is no suggestion in Youmans et al to one of ordinary skill in the art to make a TB vaccine comprising inactivated *Mycobacterium tuberculosis* in accordance with the present invention, absent impermissible reliance on the teachings in Applicants' specification.

Furthermore, page 111, second column in Youmans et al. reads:

"There is little indication from the data that immunizing activity of whole cells, whether viable or killed, was affected appreciably by being administered in Fruend's incomplete adjuvant". This is a further teaching away from the combination of reference and the presently claimed invention which is a combination of inactivated cells and adjuvant. Since the paper clearly describes very little, if any, success in administering the *M. tuberculosis* cells together with adjuvant, it certainly does not provide one of ordinary skill in the art with the necessary motivation to use an adjuvant as described

in the Schroder et al reference, absent Applicants' disclosure which again represent impermissible hindsight. That is, Youmans et al teach that an adjuvant like Freund's adjuvant does not have any improving effect on the immune response irrespective of whether the adjuvant is used together with living or heat-killed mycobacterial cells. Accordingly, a person skilled in the art would realize that the important issue in connection with provoking an immune response against M. Tuberculosis would be to use living cells and that the use of an adjuvant would not have any impact on the result.

Moreover, even though the applied Schroder reference suggests an adjuvant for use in a vaccine formulation, it does not suggest to one of ordinary skill in the art a TB vaccine. The only examples mentioned in the cited reference by Schroder are vaccines comprising diphtheria toxoid, influenza virus, and rotavirus. Applicants believe the teaching of the known prior art by Schroder and Youmans in combination do not provide any hint to use the adjuvants of Schroder in the formulation of a TB vaccine comprising **inactivated** *M. tuberculosis* cells or the success of this vaccine. In re Fritch, 23 USPQ 1780, 1784(Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.).

Schroder (1997) teaches the use of an adjuvant for stimulating the immune response, but there is no mention that such an adjuvant would be suitable for use also in situations where Freund's adjuvant has no effect or a negative effect on the immune response (e.g. such as in connection with viable or heat-killed cells from M. tuberculosis, cf. Youmans et al.). Accordingly, Applicants most respectfully submit that a person skilled in the art would based on the combined teachings in Youmans et al. and in Schroder and faced with the intention of developing an improved TB vaccine arrive at the conclusion **that living cells were of vital importance in this respect** and that it would be most unlikely that an adjuvant would be able to improve the immune response significantly. Accordingly, there would be no motivation of a person skilled in the art to try the adjuvant described by Schroder in order to improve a TB vaccine.

Even if a person skilled in the art would try, the teaching of Youmans et al and Schroder in combination would lead the skilled person to a vaccine composition

containing living cells of M. tuberculosis (cf. Youmans et al) together with the adjuvant of Schroder due to the fact that Youmans et al have shown that inactivated (heat-killed) cells of M. tuberculosis do not lead to a suitable result.

In contrast hereto, the present invention claims the use of inactivated Mycobacterium tuberculosis bacteria. **From the examples included in the specification** it is demonstrated that it is important that the bacteria are inactivated. Thus, Example 1 describes the results using two different BCGs, namely heat-killed BCG in two different adjuvant formulations and live BCG. From fig. 1 it is seen that the heat-killed BCG in the adjuvant formulation results in a positive body-weight development compared to living BCG. Furthermore, **fig. 2 shows that approx. 70% of the mice receiving heat-killed BCG together with the adjuvant formulation were still alive when the experiment ended in contrary to what was seen with the living BCG, where only 10% of the mice were alive. Example 2 and 3 support these findings, and further demonstrate the importance that the primary vaccination also is performed with inactivated BCG**.

With respect to claim 16 which provides for a TB vaccine composition wherein the monoglyceride preparation is mono-olein and the fatty acid is oleic acid, and the immunizing component is heat-killed *M. tuberculosis* bacteria, the results in these examples clearly further establishes the patentability of this subject matter. In this regard, Applicants most respectfully again direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence present by applicant and the citation of In re Soni for error in not considering evidence presented in the specification.

In conclusion, Applicants most respectfully submit that one of ordinary skill in the art, at the time of the present invention and considering the prior art as a whole would have no motivation to combine the teachings of Youmans et al. with Schroder. Even if he did he could not arrive at the present invention, namely that the use of inactivated M. Tuberculosis bacteria in a specific adjuvant would lead to a suitable immune response with the expectation of success achieved by the presently claimed invention

and set forth in the examples in the present specification. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 38-45 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder is also to be reviewed on this appeal.

The method used for vaccinating a mammal against tuberculosis as now claimed includes the administration of a vaccine composition comprising the L3 adjuvant and inactivated mycobacterium. As describes above, Youmans et al. does not teach the use of adjuvants as beneficial, and furthermore, the method using inactivated *M. tuberculosis* cells provides very poor results. This would be considered by one of ordinary skill in the art as leading one away from the presently claimed invention as there would not be an expectation of success and no motivation to carry out a vaccination as required by the claims on appeal. Obvious to try is not the standard of obviousness under 35 USC 103.

The rejection of claims 11-37 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder and further in view of Van Nest et al is another rejection to be reviewed on this appeal.

The Van Nest reference does not overcome the deficiencies of the primary and secondary reference for the reason discussed above. Van Nest et al relates to the use of any metabolizable oil for use in an adjuvant composition. There is no mention of the use of the adjuvant claimed in Van Nest et al. together with inactivated cells from M. Tuberculosis bacteria. Furthermore, the only administration route mentioned is by injection (see column 14, lines 28-33). Accordingly, the combined teachings of the three documents do not fill the gap between the combined teachings of Youmans et al and Schroder which in no way suggest any aspect of the presently claimed invention.

As discussed above and along the same line of arguments, a person skilled in the art would have no motivation to combine the teachings of Youmans and Van Nest

et al. If the teachings of Schroder and Van Nest et al are combined a person skilled in the art could at the best arrive at an adjuvant of Schroder further containing a metabolizable oil, the adjuvant being in the form of an emulsion and suitable for injection. There is no indication in Van Nest et al that a metabolizable oil used in an adjuvant can be suitable for mucosal administration. Accordingly, Applicants most respectfully submit that the combined teachings of any of the Youmans et al and Schroder, Youmans et al and Van Nest, Schroder and Van Nest nor Youmans et al and Schroder and Van Nest et al will lead a person skilled in the art to the present invention. Accordingly, it is most respectfully requested that these rejections be withdrawn.

The rejection of claims 38-46 under 35 U.S.C. 103(a) as unpatentable over Youmans et al. in view of Schroder and further in view of Van Nest et al is the last rejection to be reviewed on this appeal.

This rejection has been carefully considered but should also be reversed for the reasons discussed above. As discussed above, Applicants do not believe that a prima facie case of obviousness has been established for the claimed subject matter to a person skilled in the art in view of Youmans in combination with Schroder, at the time of the present invention. The Van Nest reference does not overcome the deficiencies of the primary and secondary reference as discussed above.

Van Nest et al relates to the use of any metabolizable oil for use in an adjuvant composition. There is no mention of the use of the adjuvant claimed in Van Nest et al. together with inactivated cells from M. Tuberculosis bacteria. Furthermore, the only administration route mentioned is by injection (see column 14, lines 28-33). Accordingly, the combined teachings of the three documents do not fill the gap between the combined teachings of Youmans et al and Schroder which in no way suggest any aspect of the presently claimed invention.

As discussed above and along the same line of arguments, a person skilled in the art would have no motivation to combine the teachings of Youmans and Van Nest et al. If the teachings of Schroder and Van Nest et al are combined a person skilled in the art could at the best arrive at an adjuvant of Schroder further containing a

metabolizable oil, the adjuvant being in the form of an emulsion and suitable for injection. There is no indication in Van Nest et al that a metabolizable oil used in an adjuvant can be suitable for mucosal administration. Accordingly, Applicants most respectfully submit that the combined teachings of any of the Youmans et al and Schroder, Youmans et al and Van Nest, Schroder and Van Nest nor Youmans et al and Schroder and Van Nest et al will lead a person skilled in the art to the present invention. Accordingly, it is most respectfully requested that this rejection be reversed on appeal.

IX. CONCLUSION

In view of the above arguments, the rejections of the claims on appeal should not be sustained. The prior art rejections should be reversed and the application passed to issue.

Respectfully submitted,

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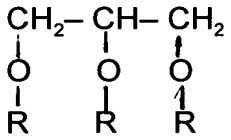
October 28, 2004

(c)(1)(viii) Claims appendix

11. A Tuberculosis (TB) vaccine composition comprising, as adjuvant, one or more substances selected from the group consisting of:

a) monoglyceride preparations having at least 80% monoglyceride content and having a formula



wherein R is H or an acyl group containing from 6 to 24 carbon atoms with the proviso that two of the R groups are H, and

b) a fatty acid with 6 to 24 carbon atoms; and

as immunizing component, inactivated *Mycobacterium tuberculosis* bacteria.

12. The TB vaccine composition according to claim 11, wherein the *M. tuberculosis* bacteria are heat or formalin killed.

13. The TB vaccine composition according to claim 11, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 90%, and the acyl chains of the monoglyceride in the monoglyceride preparation contains 8 to 20 carbon atoms.

14. The TB vaccine composition according to claim 11, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 95% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 14 to 20 carbon atoms.

15. The TB vaccine composition according to claim 11, which further comprises pharmaceutical excipients selected from the group consisting of biocompatible oils, physiological saline solutions, preservatives, osmotic pressure controlling agents, carrier gases, pH-controlling agents, organic solvents, hydrophobic agents, enzyme inhibitors, water absorbing polymers, surfactants, absorption promoters and anti-oxidative agents.

16. The TB vaccine composition according to claim 11, wherein the monoglyceride preparation is mono-olein and the fatty acid is oleic acid, and the immunizing component is heat-killed *M. tuberculosis* bacteria.

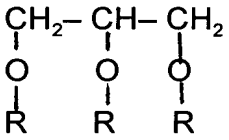
17. The TB vaccine composition according to claim 15, wherein the adjuvant further comprises soybean oil.

18. The TB vaccine composition according to claim 11, wherein the composition is formulated into a preparation for mucosal administration.

19. The TB vaccine composition according to claim 18, wherein the mucosal administration is nasal, pulmonary, oral or vaginal administration.

20. An aerosol or spray package comprising a TB vaccine composition comprising, as adjuvant, one or more substances selected from the group consisting of:

a) monoglyceride preparations having at least 80% monoglyceride content and having the formula



wherein R is H or an acyl group containing from 6 to 24 carbon atoms with the proviso that two of the R groups are H, and

b) a fatty acid with 6 to 24 carbon atoms, and

as immunizing component, inactivated *Mycobacterium tuberculosis* bacteria.

21. An aerosol or spray package according to claim 20. wherein the *M. tuberculosis* bacteria are heat or formalin killed.

22. An aerosol or spray package according to claim 20, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 90%, acyl chains of the monoglyceride in the monoglyceride preparation and contains 8 to 20 carbon atoms.

23. An aerosol or spray package according to claim 20, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 95% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 14 to 20 carbon atoms.

24. An aerosol or spray package according to claim 20, which further comprises pharmaceutical excipients selected from the group consisting of biocompatible oils, physiological saline solutions, preservatives, osmotic pressure controlling agents, carrier oases, pH-controlling agents, organic solvents, hydrophobic

agents, enzyme inhibitors, water absorbing polymers, surfactants, absorption promoters and anti-oxidative agents.

25. An aerosol or spray package according to claim 20, wherein the monoglyceride preparation is mono-olein and the fatty acid is oleic acid, and the immunizing component is heat-killed *M. tuberculosis* bacteria.

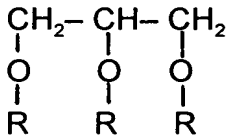
26. An aerosol or spray package according to claim 20, wherein the composition is formulated into a preparation for mucosal administration.

27. An aerosol or spray package according to claim 26, wherein the mucosal administration is nasal, pulmonary, oral or vaginal administration.

28. An aerosol or spray package according to claim 25, wherein the adjuvant further comprises soybean oil.

29. A nose-drop package comprising a TB vaccine composition comprising, as adjuvant, one or more substances selected from the group consisting of:

a) monoglyceride preparations having at least 80% monoglyceride content and having the general formula



wherein R is H or an acyl group containing from 6 to 24 carbon atoms with the proviso that two of the R groups are H, and

b) a fatty acid with 6 to 24 carbon atoms; and
as immunizing component, inactivated *Mycobacterium tuberculosis* bacteria.

30. The nose-drop package, according to claim 29, wherein the *M. tuberculosis* bacteria are heat or formalin killed.

31. The nose-drop package according to claim 29, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 90% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 8 to 20 carbon atoms.

32. The nose-drop package according to claim 29, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 95% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 14 to 20 carbon atoms.

33. The nose-drop package according to claim 29, which further comprises pharmaceutical excipients selected from the group consisting of biocompatible oils, physiological saline solutions, preservatives, osmotic pressure controlling agents, carrier gases, pH-controlling agents, organic solvents, hydrophobic agents, enzyme inhibitors, water absorbing polymers, surfactants, absorption promoters and anti-oxidative agents.

34. The nose-drop package according to claim 29, wherein the monoglyceride preparation is mono-olein and the fatty acid is oleic acid, and the immunizing component is heat-killed *M. tuberculosis* bacteria.

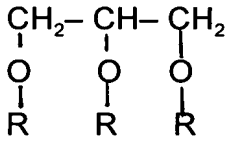
35. The nose-drop package according to claim 29, wherein the composition is formulated into a preparation for mucosal administration.

36. The nose-drop package according to claim 35, wherein the mucosal administration is nasal, pulmonary, oral or vaginal administration.

37. The nose-drop package according to claim 34, wherein the adjuvant further comprises soybean oil.

38. A method of vaccinating a mammal against Tuberculosis (TB) which comprises mucosal administration to the mammal of a protection-inducing amount of a TB vaccine composition comprising, as adjuvant one or more substances selected from the group consisting of:

a) monoglyceride preparations having at least 80% monoglyceride content and having the general formula



wherein R is H or an acyl group containing from 6 to 24 carbon atoms with the proviso that two of the R groups are H; and

b) a fatty acid with 6 to 24 carbon atoms; and

as immunizing component, inactivated *Mycobacterium tuberculosis* bacteria.

39. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, wherein the *M. tuberculosis* bacteria are heat or formalin killed.

40. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 90% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 8 to 20 carbon atoms.

41. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, wherein the adjuvant has a content of monoglyceride in the monoglyceride preparation of at least 95% and the acyl chains of the monoglyceride in the monoglyceride preparation contains 14 to 20 carbon atoms.

42. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, which further comprises pharmaceutical excipients selected from the group consisting of biocompatible oils, Physiological saline solutions, preservatives, osmotic pressure pH-controlling agents, carrier gases, pH-controlling agents, organic solvents, hydrophobic agents, enzyme inhibitors, water absorbing polymers, surfactants, absorption promoters and anti-oxidative agents.

43. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, wherein the monoglyceride preparation is mono-olein and the fatty acid is oleic acid, and the immunizing component is heat-killed *M. tuberculosis* bacteria.

44. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 38, wherein the composition is formulated into a preparation for mucosal administration.

45. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 44, wherein the mucosal administration is nasal, pulmonary, oral or vaginal administration.

46. The method of vaccinating a mammal against Tuberculosis (TB) according to claim 42, wherein the adjuvant further comprises soybean oil.